IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	:	
Bernd RIEDL et al.	:	Group Art Unit: TO BE ASSIGNED
Continuation of Application Serial No.: 09/425,229	:	Examiner: TO BE ASSIGNED
Filed: March 4, 2002	:	

For: ω-CARBOXY ARYL SUBSTITUTED DIPHENYL UREAS AS P38 KINASE INHIBITORS

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please amend the accompanying application as follows.

IN THE SPECIFICATION

Please replace the first paragraph with the following:

-- This application is a continuation of 09/425,229 filed October 22, 1999 which is a continuation-in-part of Serial Number 09/257,265 filed February 25, 1999. This application claims the benefit of the filing date of U.S. Provisional Application Serial No. 60/115,878, filed January 13, 1999. The content of these applications are incorporated herein by reference. --

Please amend page 85, third paragraph as follows.

Entry 101: 2-Amino-3-methyoxynaphthalene was synthesized as described in Method A1. According to Method C3, 2-amino-3-methoxynaphthalene was reacted with bis(trichloromethyl) carbonate followed by an aniline to form the urea.

IN THE CLAIMS

Please cancel claims 13-38 without prejudice or disclaimer.

Please amend claim 6 as follows.

6. (Amended) A method as in claim 1 wherein the condition within a host treated by administering a compound of formula I is an infectious disease selected from the group consisting of tuberculosis, Helicobacter pylori infection during peptic ulcer disease, Chaga's disease resulting from Trypanosoma cruzi infection, effects of Shiga-like toxin resulting from E. coli infection, effects of enterotoxin A resulting from Staphylococcus infection, meningococcal infection, and infections from Borrelia burgdorferi, Treponema pallidum, cytomegalovirus, influenza virus, Theiler's encephalomyelitis virus, and the human immunodeficiency virus (HIV).

Please add claims 39-59 as follows:

--39. A method for the treatment of a disease mediated by p38 comprising administering a compound selected from the group consisting of:

N-(5-*tert*-butyl-2-methoxy phenyl)-*N'*-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea;

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea and their pharmaceutically acceptable salts.

40. A method as in claim 39 comprising administering:

N-(5-tert-butyl-2-methoxy phenyl)-*N'*-(4-(4-methoxy-3-(*N*-methyl

carbamoyl)phenoxy)phenyl) urea or a pharmaceutically acceptable salt thereof.

41. A method as in claim 39 comprising administering:

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea or a pharmaceutically acceptable salt thereof.

42. A method as in claim 39 comprising administering:

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea or a pharmaceutically acceptable salt thereof.

43. A method as in claim 39 comprising administering:

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea or a pharmaceutically acceptable salt thereof.

44. A method as in claim 39 comprising administering:

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea or a pharmaceutically acceptable salt thereof.

45. A method as in claim 39 where the compound administered is a tosylate salt.

46. A method as in claim 40 where the compound administered is a tosylate salt.

47. A method as in claim 41 where the compound administered is a tosylate salt.

48. A method as in claim 42 where the compound administered is a tosylate salt.

49. A method as in claim 43 where the compound administered is a tosylate salt.

50. A method as in claim 44 where the compound administered is a tosylate salt.

51. A method for a treatment of the disease within a host selected from the group consisting of rheumatoid arthritis, osteoarthritis, septic arthritis, tumor metastasis, periodontal disease, corneal ulceration, proteinuria, coronary thrombosis from atherosclerotic plaque, aneurysmal aortic, birth control, dystrophobic epidermolysis bullosa, degenerative cartilage loss following traumatic joint injury, osteopenias mediated by MMP activity, tempero mandibular joint disease or demyelating disease of the nervous system said method comprising administering to a host a compound selected from the group consisting of:

N-(5-*tert*-butyl-2-methoxy phenyl)-*N'*-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N'*-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea;

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N'*-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea and their pharmaceutically acceptable salts.

52. A method for a treatment of the condition within a host selected from the group consisting of rheumatic fever, bone resorption, postmenopausal osteoperosis, sepsis, gram negative sepsis, septic shock, endotoxic shock, toxic shock syndrome, systemic inflammatory response syndrome, inflammatory bowel disease (Crohn's disease and ulcerative colitis), Jarisch-Herxheimer

reaction, asthma, adult respiratory distress syndrome, acute pulmonary fibrotic disease, pulmonary sarcoidosis, allergic respiratory disease, silicosis, coal worker's pneumoconiosis, alveolar injury, hepatic failure, liver disease during acute inflammation, severe alcoholic hepatitis, malaria (Plasmodium falciparum malaria and cerebral malaria), non-insulin-dependent diabetes mellitus (NIDDM), congestive heart failure, damage following heart disease, atherosclerosis, Alzheimer's disease, acute encephalitis, brain injury, multiple sclerosis (demyelation and oligiodendrocyte loss in multiple sclerosis), lymphoid malignancy, pancreatitis, impaired wound healing in infection, myelodysplastic syndromes, systemic lupus erythematosus, biliary cirrhosis, bowel necrosis, psoriasis, radiation injury/ toxicity following administration of monoclonal antibodies, host-versus-graft reaction (ischemia reperfusion injury and allograft rejections of kidney, liver, heart, and skin), lung allograft rejection (obliterative bronchitis) or complications due to total hip replacement said method comprising administering to a host a compound selected from the group consisting of:

N-(5-*tert*-butyl-2-methoxy phenyl)-*N*'-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N*'-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N*'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N*'-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea;

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N*'-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea and their pharmaceutically acceptable salts.

53. A method for treating an infectious disease within a host selected from the group consisting of tuberculosis, Helicobacter pylori infection during peptic ulcer disease, Chaga's disease resulting from Trypanosoma cruzi infection, effects of Shiga-like toxin resulting from E. coli infection, effects of enterotoxin A resulting from Staphylococcus infection, meningococcal infection, and infections from Borrelia burgdorferi, Treponema pallidum, cytomegalovirus, influenza virus, Theiler's encephalomyelitis virus, and the human immunodeficiency virus (HIV) said method

comprising administering to a host a compound selected from the group consisting of:

N-(5-*tert*-butyl-2-methoxy phenyl)-*N*'-(4-(4-methoxy-3-(*N*-methylcarbamoyl)phenoxy)phenyl) urea,

N-(2-methoxy-5-(trifluoromethyl)phenyl)-*N*'-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N*'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-*N*'-(4-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea;

N-(2-methoxy-4-chloro-5-(trifluoromethyl)phenyl)-*N*'-(3-(2-(*N*-methylcarbamoyl)-4-pyridyloxy)phenyl) urea and their pharmaceutically acceptable salts.--

REMARKS

Claims 1-12 and 49-63 are now pending in this application and are all method claims.

Respectfully submitted,

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RJT/lvb
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Please amend page 85, third paragraph as follows.

Entry 101: ~~4-Chloro-N-methyl-2-pyridinecarboxamide, which was synthesized according to Method A2, Step 3a, was reacted with 3-aminophenol according to Method A2, Step 4, to form 3-(-2-(*N*-methycarbamoyl)-4-pyridyloxy)aniline.~~ 2-Amino-3-methyoxynaphthalene was synthesized as described in Method A1. According to Method C3, 2-amino-3-methoxynaphthalene was reacted with bis(trichloromethyl) carbonate followed by ~~3-(-2-*N*-methylcarbamoyl)-4-pyridyloxy)aniline~~ an aniline to form the urea.

IN THE CLAIMS

Claims 13-48 have been canceled without prejudice or disclaimer.

Claim 6 has been amended as follows.

6. (Amended) A method as in claim 1 wherein the condition within a host treated by administering a compound of formula I is ~~an~~ an infectious disease selected from the group consisting of tuberculosis, Helicobacter pylori infection during peptic ulcer disease, Chaga's disease resulting from Trypanosoma cruzi infection, effects of Shiga-like toxin resulting from E. coli infection, effects of enterotoxin A resulting from Staphylococcus infection, meningococcal infection, and infections from Borrelia burgdorferi, Treponema pallidum, cytomegalovirus, influenza virus, Theiler's encephalomyelitis virus, and the human immunodeficiency virus (HIV).

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